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Clinical and biochemical correlates of starting "daily" hemodialysis

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Clinical and biochemical correlates of starting "daily" hemodialysis.

Background. Daily hemodialysis has been proposed to improve outcomes for patients with end-stage renal disease. There has been increasing evidence that daily hemodialysis might have potential advantages over intermittent dialysis. However, despite these potential advantages, daily hemodialysis is infrequently used in the United States, and published accounts on the technique are few.

Methods. We describe patient outcomes after increasing their hemodialysis frequency from three to six times per week in a cohort of 72 patients treated at nine centers during 1972 to 1996. Analyses of predialysis blood pressure and laboratory parameters from 6 months before until 12 months after starting frequent hemodialysis used a repeated-measures statistical technique.

Results. Predialysis systolic and diastolic blood pressures fell by 7 and 4 mm Hg, respectively, after starting frequent hemodialysis ($P = 0.02$). Reductions were greatest among patients being treated with antihypertensive medications, despite a reduction in their dosage of medications. Postdialysis weight fell by 1.0% within one month of starting frequent hemodialysis and improved control of hypertension. After the initial drop, postdialysis weight increased at a rate of 0.85 kg per six months. Serum albumin rose by 0.29 g/dl ($P < 0.001$) between months 1 to 12 of treatment with daily hemodialysis. Hematocrit rose by 3.0 percentage points ($P = 0.02$) among patients ($N = 56$) not treated with erythropoietin during this period. Two years after the start of daily hemodialysis, Kaplan–Meier analyses showed a patient survival of 93%, a technique survival of 77%, and an arteriovenous fistula patency of 92%. Vascular access patency was excellent despite more frequent use of the access.

Conclusions. These results suggest that in certain patients, daily hemodialysis might have advantages over three times per week hemodialysis.

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Hemodialysis patients dialyze intermittently and, therefore, experience repetitive cycling of body water content, serum osmolality, and dialyzable body constituents. Such cycling is an abnormal physiologic state and may contribute to morbidity and mortality among hemodialysis patients [1]. It has been proposed that uremia should be treated by frequent dialysis to reduce the magnitude of such swings in body composition [1, 2]. Despite the potential advantages of daily hemodialysis, currently, hemodialysis for end-stage renal disease (ESRD) is usually performed three times per week. Data from the United States Renal Data System show that in 1993, only 0.3% of prevalent hemodialysis patients dialyzed more than three times per week [3].

There may be other advantages to daily hemodialysis. There is increasing evidence of the beneficial effects of greater delivered doses of dialysis on patient morbidity and mortality [4, 5]. Hemodialysis is most efficient at removing solute early in the course of an individual treatment, and frequent, short hemodialysis sessions can achieve greater urea removal when the total treatment time per week is constant [6, 7].

Despite an increasing interest in daily hemodialysis, because of recognition of potential benefits of this technique, published accounts of experience with the technique are few and describe limited experience [2, 8–11]. To describe the accumulated experience, we report on new analyses of data collected from centers known to have treated patients with daily hemodialysis for over one year. Throughout this article the use of frequent hemodialysis is referred to as daily hemodialysis. In fact, the median frequency of dialysis in the 72 patients described in this study was six times per week (78% of patients), and only 14% dialyzed on a daily basis.

METHODS

Data sources and collection

Data for this study came from nine centers in Europe and the United States with experience of daily hemodialysis (the centers, principal investigators, and the number of patients at each site are listed in the **Acknowledgments** section). Data for 72 study patients were collected by dialysis unit staff in each center. After data entry and quality control, the data were transferred for analysis to Ann Arbor, Michigan, USA. Database management and analyses used the SAS statistical system (version 6.12; SAS Institute, Cary, NC, USA).

Statistical analysis

Analyses of predialysis blood pressure and laboratory values at times before and after switching from three times per week hemodialysis to daily hemodialysis used a repeated-measures technique. Generalized linear regression models were fitted using the "PROC MIXED" procedure of the SAS statistical program. Each model allowed estimation of the trend (slope) in the parameter of interest while the patient was on conventional center hemodialysis, allowed the average level to change at the time of switch to daily hemodialysis, and allowed an estimation of the trend after switching to daily hemodialysis. The analysis was confined to the period from 6 months before to 12 months after switching to daily hemodialysis. The time points during this period were 3 and 6 months before switching to daily hemodialysis, the time of switch, and 1, 3, 6, 9, and 12 months after switching.

Analysis of the proportions of patients receiving antihypertensive agents and phosphate binders between 1 month before and until 12 months after switching to daily hemodialysis used McNemar's test for the equality of proportions in matched samples.

Analyses of patient survival, technique survival, time to first hospitalization, and vascular access failure from the time of starting daily hemodialysis were made by the Kaplan–Meier method. An intent-to-treat method was used to analyze patient survival so that for the purposes of the analyses, the original treatment assignment was unchanged if the patient stopped daily hemodialysis and resumed conventional hemodialysis. Each death was considered an event, and observations were censored at the end of follow-up or at transplantation.

Both death and restarting conventional hemodialysis were considered as events for analyses of technique survival; observations were censored at the end of follow-up and at transplantation. However, in three instances, patients were switched to daily hemodialysis and then back to conventional dialysis as part of a planned study. Follow-up of technique survival for these patients was censored on the date of their planned return to treatment with conventional hemodialysis.

One center (Catanzaro, Italy) provided only data on patients who had survived for at least one year after switching to daily hemodialysis. Separate sensitivity analyses were therefore performed to determine the effect of exclusion of patients from this center and all patients with less than one-year experience of daily hemodialysis on the outcome. First, patient and technique survival was reanalyzed after excluding this center. Second, patient and technique survival was reanalyzed with all centers included, but with the analysis starting at one year after switching to daily hemodialysis. Patient and technique survival was compared between patients treated with daily hemodialysis at home versus in a dialysis center using the log-rank statistic.

For vascular access survival, the dependent variable in the analysis was time from start of daily hemodialysis until the first vascular access failure identified in the medical record; observations were censored at death, transplantation, return to conventional hemodialysis, or the end of patient follow-up. A vascular access failure was considered to have occurred when the medical record indicated that an access thrombosis or infection developed, when access blood flow was judged insufficient to allow the prescribed dialysis treatment, or when a surgical procedure on the access was performed.

For the analysis of hospitalization, the dependent variable was time from the start of daily hemodialysis until the first hospitalization. The analysis was censored at death, transplantation, return to conventional hemodialysis, or end of patient follow-up. A sensitivity analysis considered an unplanned return to conventional hemodialysis as an event.

RESULTS

Data were available for 72 patients who started daily hemodialysis between 1972 and 1996 (the median year was 1988). The median patient age was 47 years (range 13 to 70 years). Seventy-four percent were male, and 97% were of the white race. The cause of ESRD was glomerulonephritis in 48.6% of cases, polycystic kidney disease in 23.6%, interstitial nephritis in 8.3%, diabetes mellitus in 6.9%, and other causes in 12.6%.

The median period of treatment with conventional hemodialysis prior to switching to daily hemodialysis was 24 months; 81% of patients were treated with conventional hemodialysis for more than 6 months and 67% for longer than 12 months. Patients were treated with daily hemodialysis for a median of 24 months (range 4 to 158 months); 32% of patients were treated with daily hemodialysis for less than 12 months. The median predialysis blood urea nitrogen (BUN) value at three months before starting daily hemodialysis was 98 mg/dl, and at three months after starting daily hemodialysis, it was 79 mg/dl. Details of the dialysis prescription before and then on starting daily hemodialysis are shown in Table 1.

The most common reason given for starting daily hemodialysis was lifestyle or employment (37.9%). Patients also started daily hemodialysis to allow better control of

Table 1. Dialysis prescription before (conventional) and on starting daily hemodialysis

Parameter (median value unless stated)	Conventional hemodialysis	Daily hemodialysis
Number of treatments per week (range)	3 (2–4)	6 (5–7)
Duration of each hemodialysis treatment *hours* (range)	4.0 (2.5–8.0)	1.5 (1.1–3.0)
Total hemodialysis treatment time per week *hours*	12	10.5
Percent synthetic or semisynthetic dialyzer membrane	42	51
Dialyzer membrane surface area m^2 (range)	1.3 (0.9–2.1)	1.3 (0.9–2.1)
Dialyzer blood flow rate *ml/min*	275	285
Dialysate flow rate *ml/min*	500	500
Percent HCO_3^- dialysate	83	92
Percent single pass dialysate circulation	95	56

Table 2. Levels and trends before and after change from conventional to daily hemodialysis (HD) for blood pressure, weight, albumin, and hematocrit

Parameter	Conventional hemodialysis			Start of daily HD		Daily hemodialysis	
	Change per 6 months	*P* value	Mean prior to starting daily HD	Change	*P* value	Change per 6 months	*P* value
Blood pressure (BP)							
All patients							
Predialysis systolic BP	−2	0.93	144	−7	0.02	−7	0.21
Predialysis diastolic BP	0	0.93	86	−4	0.02	−4	0.07
Subgroup of patients treated with antihypertensive medications ($N = 35$)							
Predialysis systolic BP	−4	0.49	163	−13	<0.01	−7	0.28
Predialysis diastolic BP	−3	0.37	94	−7	0.02	−3	0.33
Weight							
Post-dialysis weight *kg*	−0.44	0.18	63.3	−0.63	0.03	0.85	0.02
Albumin							
Serum albumin *g/dl*	−0.18	0.01	3.88	0.2	<0.01	0.1	<0.001
Hematocrit %							
All patients	0.2	0.71	27.9	1.7	0.002	0.9	0.31
Subgroup of patients not treated with erythropoietin ($N = 56$)	0.2	0.72	27.5	1.8	0.004	1.5	0.02

hypertension (13.8%), to avoid intradialytic hypotension (15.5%), because of other medical reasons (24.1%), because of preference, or as part of a planned study (8.6%). After switching to daily hemodialysis, 58% of patients ($N = 42$) dialyzed at home, and 42% ($N = 30$) dialyzed in a hemodialysis center. Patients who dialyzed at home after switching were more likely than patients who continued to dialyze in a center to have changed to daily hemodialysis for lifestyle or employment reasons (57 vs. 9%, $P < 0.01$), and less likely to have switched for better control of hypertension, avoidance of intradialytic hypotension, or other medical reasons (40 vs. 74%, $P = 0.01$).

Trends in postdialysis weight

The postdialysis weight declined by 0.44 kg ($P = 0.18$) during the six months that patients were treated with conventional dialysis (Table 2). The mean postdialysis weight immediately prior to starting daily hemodialysis was 63.3 kg. On starting daily hemodialysis, postdialysis weight decreased by 0.63 kg ($P = 0.03$), a reduction of 1.0%. Thereafter, the postdialysis weight increased by 0.85 kg per six months ($P = 0.02$) while the patients were treated with daily hemodialysis.

Trends in blood pressure

The changes in predialysis systolic and diastolic blood pressures that occurred over the periods before and after patients switched from conventional hemodialysis to daily hemodialysis are shown in Figure 1 and Table 2. There was a statistically significant reduction in both systolic blood pressure (−7 mm Hg, $P = 0.02$) and diastolic blood pressure (−4 mm Hg, $P = 0.02$) at the time of switch. This reduction was greater among the 49% of patients receiving antihypertensive medications at the time of switch to daily hemodialysis; systolic blood pressure fell by −13 mm Hg ($P < 0.01$), and diastolic blood pressure fell by −7 mm Hg ($P = 0.02$). There was no corresponding increase in these medications, but instead, a statistically significant reduction in the number of antihypertensive medications prescribed during the 12 months after switching to daily hemodialysis (Fig. 2).

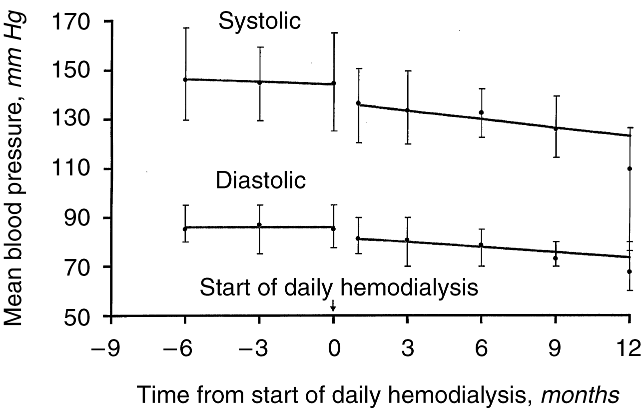

Fig. 1. Predialysis systolic blood pressure (SBP) and diastolic blood pressure (DBP) in patients (N = 72) from 6 months before until 12 months after starting daily hemodialysis. Plots show the mean SBP and DBP at each time point (●), the interquartile range (25th to 75th percentiles), and the fitted line from the regression model. SBP fell 7 mm Hg (P = 0.02), and DBP fell 4 mm Hg (P = 0.02) on starting daily hemodialysis (time 0). The slopes of the fitted lines after starting daily hemodialysis were not statistically different from zero (SBP = −7 mm Hg per 6M, P = 0.21; DBP = − 4 mm Hg per 6M, P = 0.07).

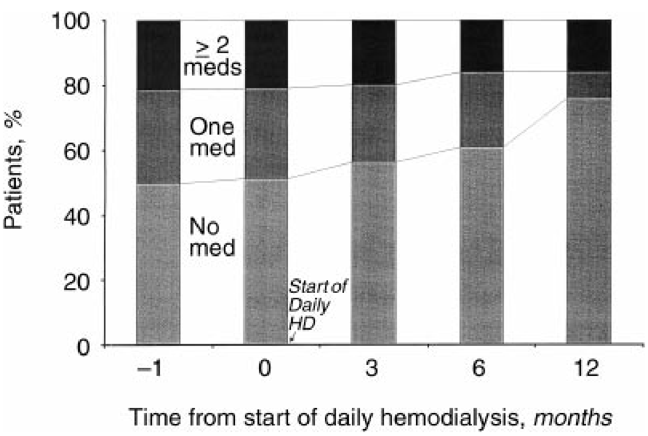

Fig. 2. Percentages of patients (N = 72 at time 0) prescribed 0, 1, and 2 or more antihypertensive medications at 0 and 1 month before and at 3, 6, and 12 months after starting daily hemodialysis.

The percentage of patients receiving no antihypertensive medications increased from 54 to 61% at six months and 75% at one year after the switch to daily hemodialysis. The fraction of patients receiving more than one antihypertensive medication also decreased.

Trends in serum albumin and cholesterol

The estimated parameters indicated that during the period of treatment with conventional hemodialysis, the serum albumin decreased by 0.18 g/dl per six months (P = 0.01) to a mean level of 3.88 g/dl immediately prior to starting daily hemodialysis. The mean serum albumin level rose 0.2 g/dl (P = 0.004) on starting daily hemodialysis, and thereafter, it rose by 0.1 g/dl per six months

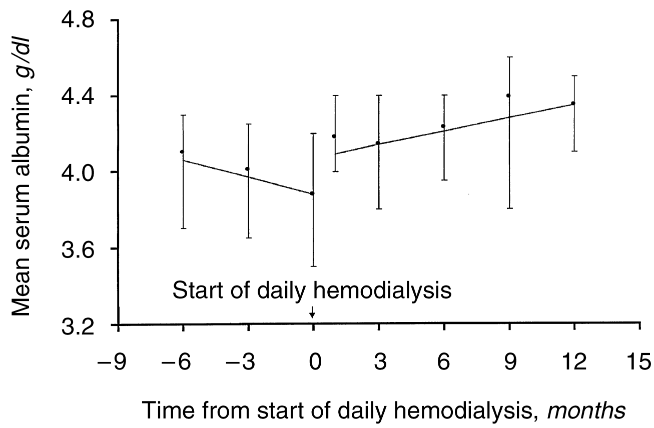

Fig. 3. Changes in predialysis serum albumin levels for patients (N = 68) from 6 months before until 12 months after starting daily hemodialysis. Plot shows the mean serum albumin level (●), the interquartile range (25th to 75th percentiles), and the fitted line from the regression model.

($P < 0.001$) to 4.35 g/dl at one year after changing hemodialysis modality (Table 1 and Fig. 3).

The mean serum cholesterol was 183 mg/dl immediately prior to switching to daily hemodialysis. There were no statistically significant trends in serum cholesterol before or after increasing the dialysis frequency; no change in level at the time of switch was observed.

Trends in hematocrit

There was no statistically significant trend in hematocrit levels during the six months before changing to daily hemodialysis among all study patients (Table 2). The mean hematocrit immediately prior to starting daily hemodialysis was 27.9%. The hematocrit increased by 1.7 to 29.7% (P = 0.002) after starting daily hemodialysis. An apparent further increase in hematocrit during the subsequent 12 months on daily hemodialysis of 0.9% per six months to a level of 31.5% at 12 months was not statistically significant (P = 0.3). Excluding four patients who had a blood transfusion during either the 6 months prior to changing to daily hemodialysis or in the 12 months following the switch did not change these results substantially.

Fifty-six patients were not receiving erythropoietin at the time of change of treatment frequency. When the analysis was confined to these patients, hematocrit rose by 1.5% per six months (P = 0.02) during the treatment period with daily hemodialysis. Sixteen patients were receiving erythropoietin when they started daily hemodialysis; the median dose of erythropoietin was 8000 units per week at this time. Three months later, the median dose was 4000 units; at 6, 9, and 12 months, the median erythropoietin doses were 4000, 4000, and 5000 units, respectively.

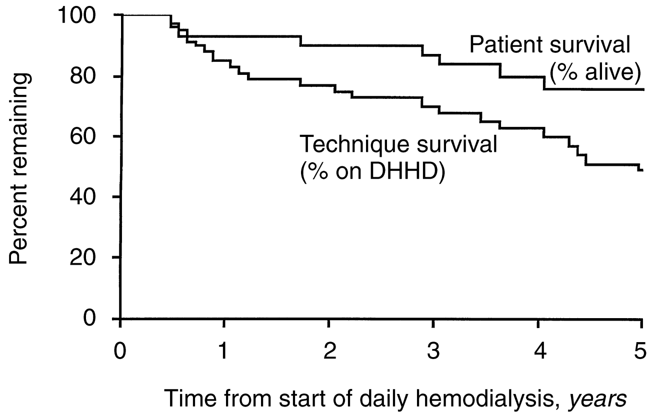

Fig. 4. Kaplan–Meier analysis of patient and technique survival starting when patients began daily hemodialysis (N = 71). Patient survival was analyzed as time until death; observations were censored at the end of follow-up or transplantation. At five years, 17 patients remained in the analysis. Technique survival was analyzed as time until an unplanned return to conventional hemodialysis or until death. Observations were censored at the end of follow-up, transplantation, or on planned switch back to conventional hemodialysis. At five years, 10 patients remained in the analysis.

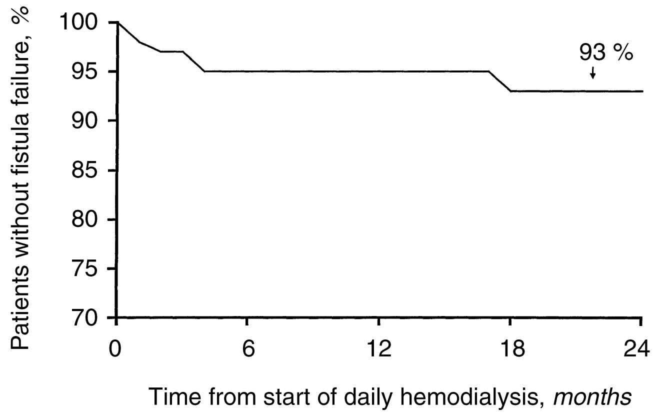

Fig. 5. Kaplan–Meier analysis of AV fistula survival among patients with a fistula on starting daily hemodialysis (N = 63). AV fistula survival was analyzed as the time from when patients started daily hemodialysis until an access thrombosis, infection, or surgery occurred or until the access blood flow was inadequate for hemodialysis. Observations were censored at death, transplantation, return to conventional hemodialysis, or the end of patient follow-up. At 24 months, 34 patients remained in the analysis.

Calcium phosphate metabolism

There were no significant changes in the average predialysis level of serum calcium or phosphate while the patients were being treated with either conventional or daily hemodialysis. The proportion of patients who did not require any medication to bind dietary phosphate did not change significantly over either treatment period.

Patient and technique survival

Kaplan–Meier survival curves of patient and technique survival for daily hemodialysis are shown in Figure 4. Patient and technique survival differed between patients dialyzed at home and in a dialysis center. Two-year patient survival (independent of switching to conventional hemodialysis) among those patients who dialyzed at home was 100% and was 81% among those who dialyzed in a dialysis center (P = 0.02); overall patient survival was 93% at two years. Two years after starting daily hemodialysis, 95% of patients dialyzed at home were still being treated with daily hemodialysis, compared with 54% of patients who dialyzed in a dialysis center ($P < 0.001$). The overall two-year technique survival was 77%.

In a series of sensitivity analyses, patient survival was estimated after exclusion of the center in Catanzaro, Italy, and also starting at one year after switching to daily hemodialysis. Patient survival after exclusion of this center was 92% at two years. In a separate analysis beginning one year after the switch, patient survival was 93% two years later.

Vascular access use and patient hospitalization

The vascular access for dialysis immediately prior to changing to daily hemodialysis was an arteriovenous (AV) fistula for 64 patients (94.1%); three patients dialyzed via an AV graft (4.4%) and one by a catheter (1.5%). Access type was not recorded for four patients. Seventeen (27%) of the 64 fistula patients dialyzed via a single blood access needle, and 46 (72%) dialyzed via two needles (percentages exclude one patient with an unknown number of needles).

Prior to starting daily hemodialysis, there were 14 recorded events in 12 patients, indicating an access failure during 606 months of follow-up (0.28 events per patient year). After patients started daily hemodialysis, there were 13 events recorded in 11 patients, indicating an access failure during 2864 months of follow-up (0.05 events per patient year), which indicates a statistically significant lower access failure rate with daily hemodialysis ($P <$ 0.001). Vascular access survival for patients with an AV fistula at the time of switch to daily hemodialysis was 93% at two years after the switch, as shown in Figure 5.

Survival analysis of hospitalization data showed that at two years after starting daily hemodialysis, 53% of patients had been admitted to a hospital at least once.

Sensitivity analyses

Because the analyses of technique survival showed that patients who dialyzed in a dialysis center were more likely to stop daily hemodialysis, a series of sensitivity analyses were performed to examine whether earlier dropout among these patients altered the trends noted in blood pressure, postdialysis weight, hematocrit, and serum albumin.

Among patients who dialyzed at home ($N = 42$), the hematocrit rose by 0.4% per six months (P = NS) after switching to more frequent hemodialysis (versus 0.9% among all patients). The rise in hematocrit was 0.9% per six months ($P = 0.06$) among those patients who dialyzed at home and who were not treated with erythropoietin at the time of switch (vs. 1.5% among all 56 patients in the study who were not treated with erythropoietin).

Serum albumin rose by 0.13 g/dl per six months ($P = 0.003$), after switching to daily hemodialysis, among patients who dialyzed at home (vs. 0.1 g/dl among all patients). Postdialysis weight rose by 0.4 kg per six months (P = NS) in patients who dialyzed at home (same as among all patients). Systolic blood pressure decreased by 12 mm Hg ($P < 0.001$) within a month of switching to daily hemodialysis in patients who dialyzed at home (vs. 7 mm Hg among all patients). At the same time point, diastolic blood pressure decreased significantly ($P = 0.001$) by 6 mm Hg (vs. 4 mm Hg among all patients).

DISCUSSION

There is an increasing interest in daily hemodialysis as a means of allowing more physiological control of body fluid and electrolyte composition and of providing lower peak toxin levels without increasing total weekly dialysis duration. We present data from a series of 72 patients, the majority of whom dialyzed at home, whose median dialysis frequency was increased on average from three to six treatments per week. The experience of nine centers with switching 72 patients from conventional hemodialysis to daily hemodialysis provides numerous new insights. We observed changes in important clinical and biochemical parameters, both within one month of the change in dialysis frequency and then during the subsequent 12 months.

Effect on control of hypertension

Extracellular volume overload contributes substantially to hypertension in hemodialysis patients, and improved achievement of "dry weight" allows better blood pressure control. We found a reduction in both predialysis systolic and diastolic blood pressure within one month of starting daily hemodialysis. Subgroup analysis showed that the greatest reduction in blood pressure on starting daily hemodialysis took place among patients requiring treatment with antihypertensive medications. The reductions in blood pressure among patients not on antihypertensive medications were of smaller magnitude and not statistically significant.

These changes in predialysis systolic and diastolic blood pressure soon after switching to daily hemodialysis likely reflect a reduction in predialysis extracellular fluid excess caused by the shorter interdialytic interval. Additionally, there was a 1.0% fall in the postdialysis weight observed on changing to daily hemodialysis. Thus, the increase in dialysis frequency likely allowed ultrafiltration to a lower postdialysis weight.

During the 12 months subsequent to starting daily hemodialysis, there was a downward trend in systolic and diastolic blood pressures that did not reach statistical significance. However, during the same period, the number of antihypertensive medications prescribed to patients also decreased significantly, both clinically and statistically. In the aggregate, the reduction in the intensity of treatment for hypertension combined with the reduction in systolic and diastolic blood pressure suggests a strong beneficial effect of daily hemodialysis on the control of hypertension compared with conventional hemodialysis.

Charra et al have shown that prolonged three-times weekly hemodialysis resulted in improved blood pressure control [12]. Prolonged hemodialysis likely allows a lower postdialysis weight to be achieved, without hemodynamic instability, through use of low ultrafiltration rates. Our results suggest that a similar effect can be produced by daily hemodialysis with short, but frequent, periods of ultrafiltration, avoiding the degree of extracellular volume overload present with conventional three-times weekly hemodialysis.

Daily hemodialysis may also have advantages for patients who have hemodynamic instability during conventional dialysis. Increasing the frequency of dialysis may allow effective ultrafiltration without intradialytic hypotension. Sixteen percent of patients in our study switched to daily hemodialysis to allow more frequent ultrafiltration with the goal of avoiding hypotension. The number of hypotensive events recorded per patient per month showed a statistically significant decline after changing to frequent hemodialysis.

Effect on hematocrit and biochemical measurements

The shortened interdialytic interval with daily hemodialysis leads to less volume excess predialysis. Thus, blood samples taken prior to dialysis are likely less diluted in patients dialyzing more frequently. Additionally, we have postulated that ultrafiltration to a lower postdialysis weight may explain changes in blood pressure seen within one month of cross-over to daily hemodialysis. The combined effect of these processes may explain the changes in serum albumin and hematocrit seen shortly after starting daily hemodialysis.

Hematocrit. It has been reported that an increase in the dose of hemodialysis in patients with ESRD is associated with an increase in hematocrit [13, 14]. In our study, overall, an apparent rise in hematocrit level on starting daily hemodialysis was not statistically significant. When the analysis was limited to only those patients not treated with erythropoietin, the hematocrit increase of 1.5% per six months during the first year of daily hemodialysis was statistically significant. Among patients treated with erythropoietin, the dose prescribed was reduced after starting daily hemodialysis, also suggesting an improvement in their anemia and perhaps an increased responsiveness to the drug. This finding may be related to better control of uremia, as suggested previously [13]. This suggests that among erythropoietin-treated patients, the magnitude of the increase in the hematocrit associated with more frequent dialysis would likely have been larger had the dose of erythropoietin been kept constant. The rate of blood transfusions before and after a change of hemodialysis frequency could also confound the relationship of dialysis method with hematocrit. The rate of blood transfusions was higher before starting daily hemodialysis, and thus, the effect of such a potential bias would reduce, rather than enhance, the observed effect of dialysis method on hematocrit. Because only a few patients received blood transfusions either before or after starting daily hemodialysis, a confounding effect of blood transfusion is likely unimportant.

Albumin. Low serum albumin is an important predictor of mortality in dialysis patients [4]. We found a statistically significant decline in serum albumin during the six months of prior conventional hemodialysis. An early increase in serum albumin, after the change to daily hemodialysis, was followed with a further increase in serum albumin during the next 12 months. Although the increase in serum albumin concentration within the first month of starting daily hemodialysis may reflect less dilution of the predialysis blood sample because of the shorter interdialytic interval, the subsequent rise in serum albumin concentration over the next 12 months appears to reflect an actual increase. This is supported by the observation that during this period, the postdialysis weight was increasing, not falling. Both the increasing serum albumin concentration and postdialysis weight independently suggest that nutritional status improves with daily hemodialysis.

Serum phosphate. Our data show no statistically significant changes in calcium or phosphate level before or after starting daily hemodialysis. We also found no statistically significant reduction in the number of phosphate binders prescribed to patients following the switch to daily hemodialysis. Phosphate is poorly removed by hemodialysis. Pierratos, Ouwendyk, and Franceur recently reported that all 12 patients who started frequent slow nocturnal home hemodialysis in their program were able to stop taking phosphate-binding medications [10]. This observation may be explained by the substantially longer duration of dialysis ranging from 48 to 70 hours per week.

Patient survival

Overall, patient survival in this study was 93% at two years after switching to daily hemodialysis. It is likely that this high survival rate in part reflects the effect of selection of patients who switched to daily hemodialysis, but who dialyzed at home. This hypothesis is supported by the observed difference in two-year survival rates between patients who dialyzed at home versus those who were treated with daily hemodialysis in a dialysis center (100 vs. 82%).

We have previously shown, in a random national sample of hemodialysis patients in the United States, that patients who start standard home hemodialysis are younger, have fewer comorbid conditions, and have higher serum albumin values when they start dialysis [15]. In this study, patients who dialyzed at home when they switched to daily hemodialysis were marginally younger than patients dialyzing in a dialysis center (median age 46 vs. 48.5 years). However, patients who dialyzed at home were more likely to have changed to daily hemodialysis for lifestyle or employment reasons rather than medical reasons. They were less likely to have switched to allow better control of hypertension or to avoid intradialytic hypotension, suggesting that they had less cardiovascular comorbidity.

Technique survival

The fraction of patients remaining on the daily hemodialysis schedule (technique survival) also was higher for patients who dialyzed at home than for those who dialyzed in a dialysis center (95 vs. 54% at two years). Poorer technique survival among patients dialyzing daily within a dialysis unit may reflect the increased time per week spent traveling to and from the dialysis unit. We found that with frequent hemodialysis, the total dialysis time per week was decreased, on average, by about 1.5 hours because the duration of each of the six sessions was slightly less than half that of the three sessions of conventional hemodialysis. However, for those patients dialyzing in a center, the amount of time spent traveling to and from the dialysis unit would approximately double with daily hemodialysis. Data from Wave-2 of the U.S. Renal Data System Dialysis Morbidity and Mortality Study, a national random sample of U.S. patients starting chronic hemodialysis during 1996, indicate that 56% of hemodialysis patients spend over 30 minutes traveling to and from their dialysis unit for a single hemodialysis treatment (F.K. Port, personal communication). The opportunity costs associated with this travel time for a working hemodialysis patient dialyzing six times per week at a dialysis center are likely to be high. We feel that daily hemodialysis in dialysis centers is likely to only be an option for patients with easy access to a nearby dialysis center. To avoid a substantial dropout rate from daily hemodialysis, it is likely that the majority of patients will need to be trained to dialyze at home at times convenient to their schedule.

Vascular access failure

Ninety-three percent of patients in this study had an AV fistula for hemodialysis vascular access. This high percentage reflects, in part, the practice in Europe and likely the selection of younger, fitter, and nondiabetic patients who have greater odds of receiving an AV fistula [16].

For most patients, daily hemodialysis requires a doubling in the number of times per week dialysis needles are placed in the vascular access. A potential barrier to introduction of the technique of daily hemodialysis is the concern that the rate of access failure may be higher because of trauma to the access as a result of more frequent dialysis needle insertion. We did not find a higher rate of vascular access failure among patients who switched to daily hemodialysis; rather, the reported vascular access failure rate fell from a relatively low rate (by U.S. standards) of 0.28 per patient year to 0.05 per patient year after starting daily hemodialysis.

We also report vascular access survival among those patients with an AV fistula. At one year, the AV fistula patency rate, without operative intervention, was 95%. These results are superior to those shown previously for AV fistula survival in a random national sample of U.S. hemodialysis patients incident in 1990, even for a subgroup of nondiabetic patients [17]. Our results of vascular access failure before and after switching to daily hemodialysis and the AV fistula survival rate following switch should be interpreted with caution. These data are limited because of the small patient sample size; only five patients actually had a reported access failure.

Why should the rate of AV fistula failure be low when the vascular access is used twice as often? One possibility is that AV fistula failure depends on the person cannulating the access. The majority of patients in this study dialyzed at home and either they or their partner cannulated the access. It may be that cannulation performed consistently by one person (the patient or their partner) leads to fewer thrombotic or infectious complications than cannulation by a series of dialysis unit personnel. The observed reduction in hypotensive episodes during dialysis may also reduce access failure from thrombosis by avoiding reduced access blood flow. It is also possible that the change to daily anticoagulation reduces the rate of access thrombosis.

Limitations

The data for this study were obtained from retrospective data collection. It was not a preplanned prospective study, and thus, there was no uniform protocol for switching patients to daily hemodialysis. Such a retrospective analysis is vulnerable to the effects of bias, confounding, and the effects of temporal changes in practice pattern. We have sought to address these issues in our analyses.

A major strength of this study is the cross-over design; patients are their own controls. The analysis method preserves this matching, allowing the comparison of blood pressure and laboratory data within individual patients between the periods of treatment with conventional and daily hemodialysis.

We have no representative information on the delivered dose of dialysis for the cohort of patients as a large majority started daily hemodialysis before the measurement of delivered dose of hemodialysis became part of routine clinical practice. We did observe a reduction in the total hemodialysis treatment time from 12 to 10.5 hours per week. Increasing the frequency of hemodialysis is an effective way of increasing the dialysis efficiency and likely offsets the reduction in total treatment time per week [6]. In a study comparing daily hemodiafiltration for nine hours per week to three times per week conventional hemodiafiltration for 12 hours per week, the time averaged blood urea nitrogen concentration did not change despite a 25% reduction in total treatment time per week [18]. Therefore, in our study, despite a 13% reduction in the total weekly hemodialysis treatment time, the total amount of urea removed per week likely increased on starting daily hemodialysis. Clearance of larger molecular weight substances may also be increased with daily therapy. In the same study the time averaged concentration of β_2 microglobulin decreased by 42% on starting daily hemofiltration [18].

Unlike conventional three times per week hemodialysis, there are no agreed standards on what constitutes an adequately delivered dose for daily hemodialysis. It is clear that Kt/V values per treatment cannot be compared between conventional and more frequent hemodialysis by summing over one week Kt/V values for individual treatments. The total weekly Kt/V required to remove the same mass of urea is less for a patient dialyzed six times per week than a patient dialyzed three times per week [6]. Until standards for hemodialysis adequacy for daily hemodialysis have been derived from clinical studies, we would suggest that the delivered dose of hemodialysis for a patient treated on a daily schedule should be unequivocally greater than the generally accepted U.S. minimum target of a Kt/V of 1.2. We would view daily hemodialysis as an opportunity to provide a greater dose of hemodialysis through increased efficiency. We strongly caution against using the increased efficiency of daily hemodialysis to reduce the total hemodialysis treatment time per week.

We have postulated that on starting daily hemodialysis, the delivered dose of dialysis increased leading to an increase in hematocrit and serum albumin. The median predialysis blood urea nitrogen concentration among the cohort of patients was 98 mg/dl at three months before starting daily hemodialysis. It is possible that during the period of treatment with conventional hemodialysis, the delivered dose of hemodialysis was low. Changes in serum albumin and hematocrit of the magnitude we observed in this study may be of smaller magnitude or may not occur if patients currently treated with a high dose of conventional hemodialysis switch to daily treatment. Patients who switched to daily hemodialysis were not chosen at random but, rather, were selected. Patients who chose or are chosen to dialyze at home are generally younger and more fit. We have previously described the magnitude of such selection in incident U.S. patients who start conventional home hemodialysis [15]. The effects of such selection can be seen in patient and technique survival, which likely would have been lower among a less selected cohort. However, such selection should not effect the temporal changes noted in blood pressure and laboratory values. Indeed, it is possible that the observed changes may have been greater among sicker patients.

We depended on physicians in each dialysis unit to identify patients who switched to daily hemodialysis and to retrieve their medical records. It may be more difficult to identify patients who only spend a short period on daily hemodialysis because of an adverse outcome. Patients at one center were only reported if they had switched to and then continued on daily hemodialysis for one year. When patients have to survive for a period to be included in a study, those patients with worse outcomes may be excluded. However, sensitivity analyses in which this center was either removed or else where survival was calculated starting at one year after switching to daily hemodialysis showed similar results to the main analysis.

Whether our findings are correct can only be proven conclusively by a randomized prospective trial comparing daily home hemodialysis with conventional center hemodialysis. Although frequently called for, prospective trials are expensive in time and funding. Frequently, the results of such trials are not available until after the introduction and widespread use of new technologies or treatment methods. Often, in the absence of prospective data, we must rely on the results of observational research to decide whether to adopt a new treatment method or technology.

In view of the encouraging results reported here and the development of automated dialysis machines designed specifically for home use [19, 20], it is likely that in the next few years, increasing numbers of patients will be switched to daily home hemodialysis. In the absence of a randomized clinical trial, we would urge investigators who are considering changing patients to daily home hemodialysis to consider collaborating in a registry with prospective data collection, so that the data necessary to confirm our findings can be collected prospectively and disseminated to clinicians and patients.

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